

1/59

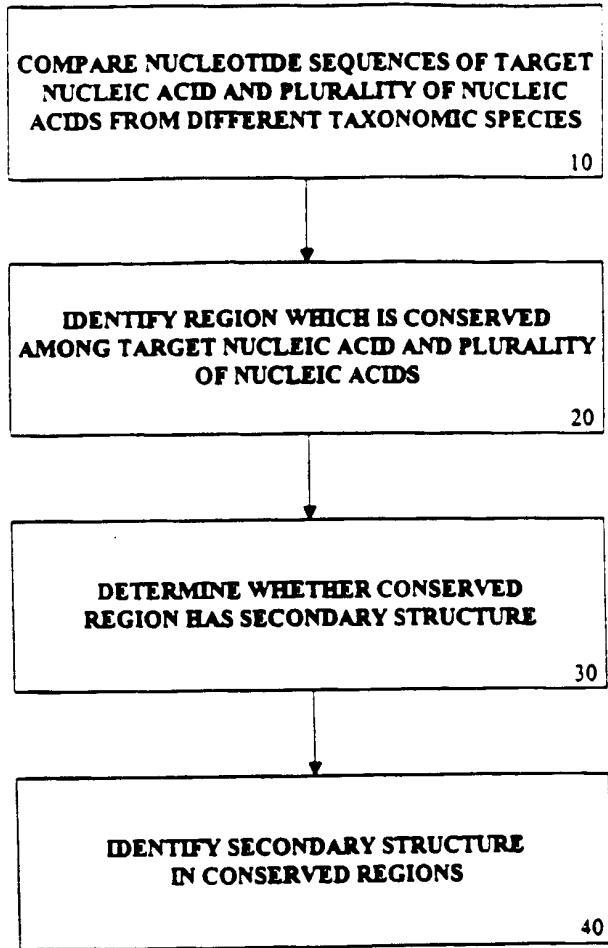


FIGURE 1

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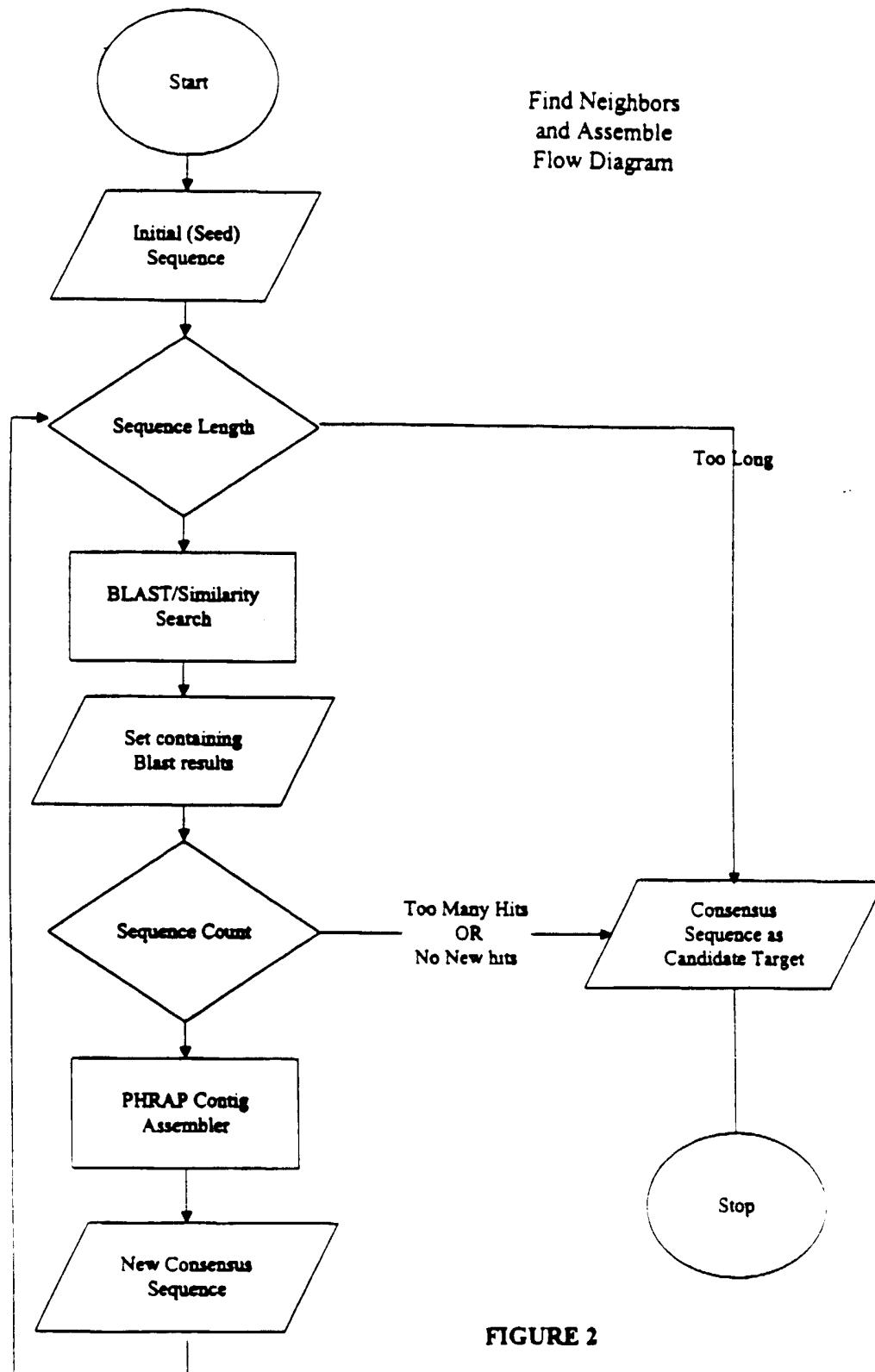


FIGURE 2

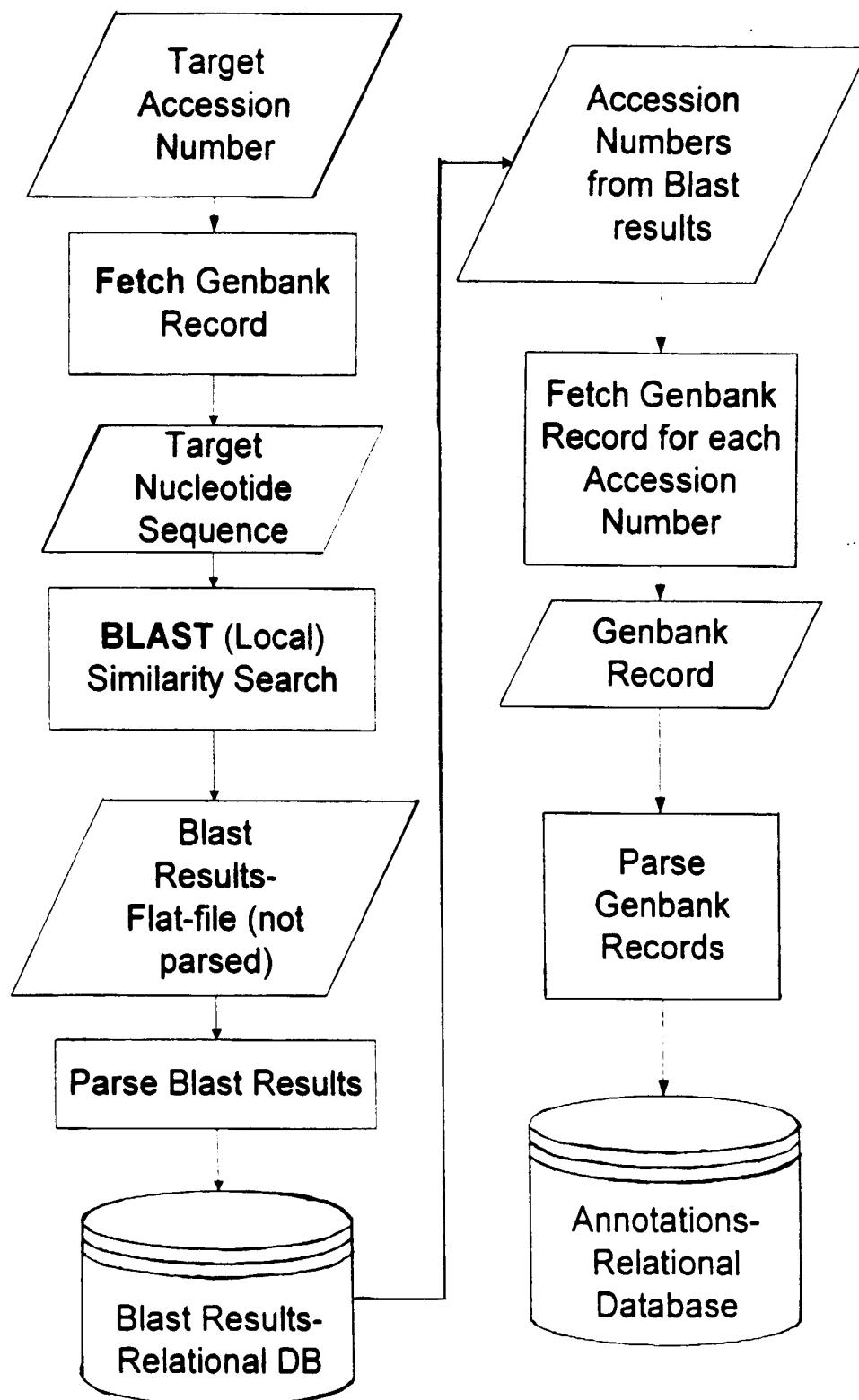


Figure 3

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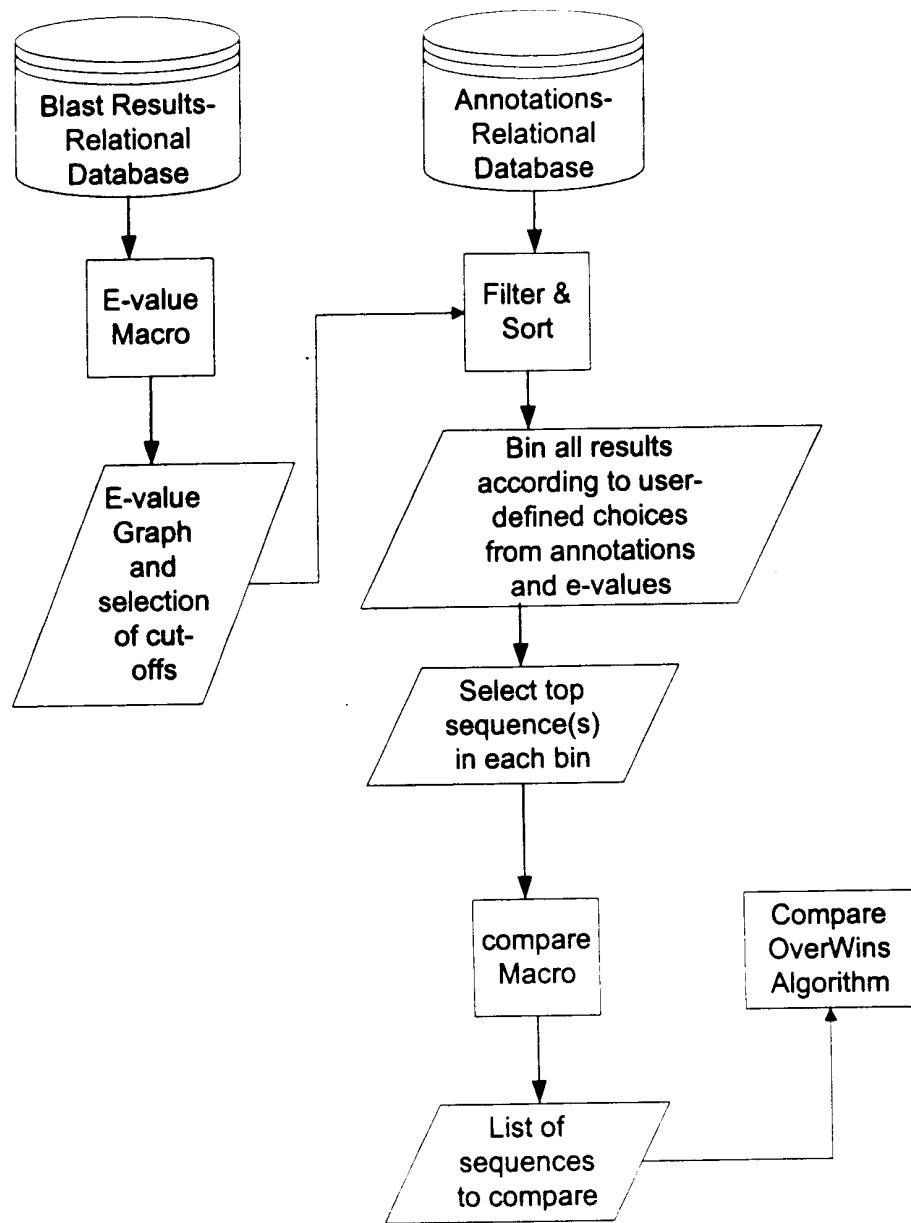


FIGURE 4

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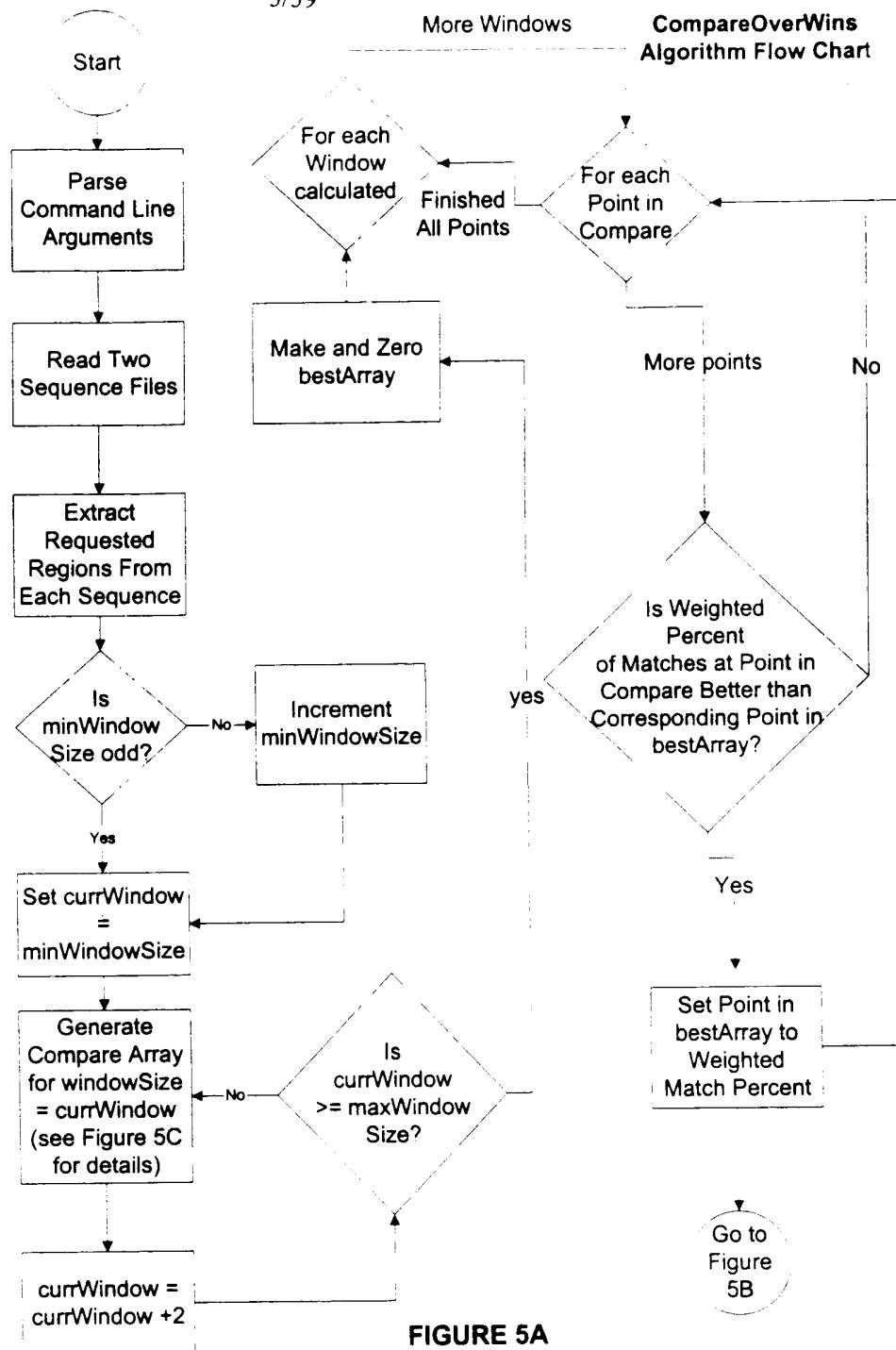


FIGURE 5A

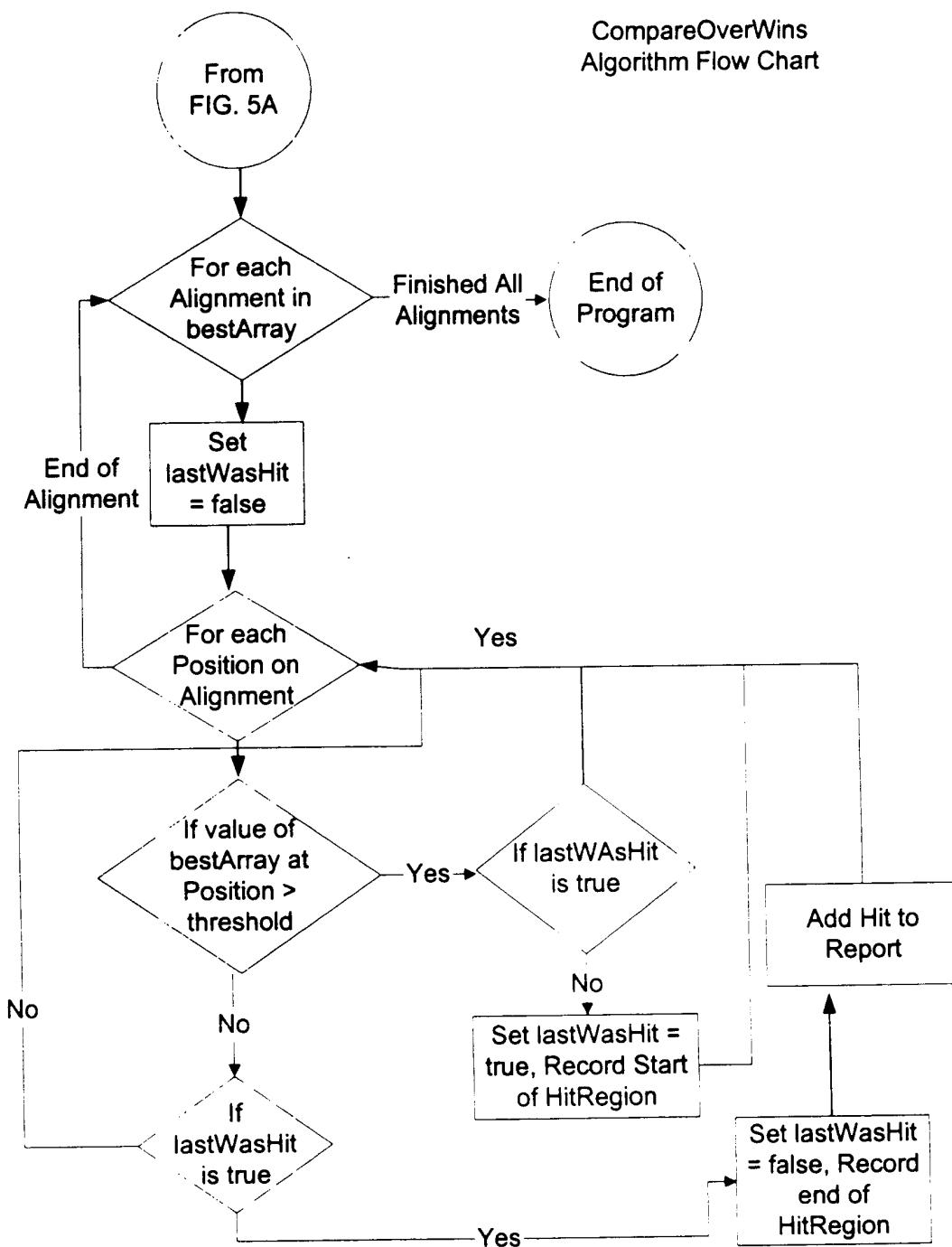


FIGURE 5B

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Input:
 Sequence A length a
 Sequence B length b
 Window Size

CompareOverWins
Algorithm Flow Chart
Basic Compare

Output:
 Array of size a by b of unsigned chars (0-255)
 Each point represents the number of matches in the
 window at that alignment and position

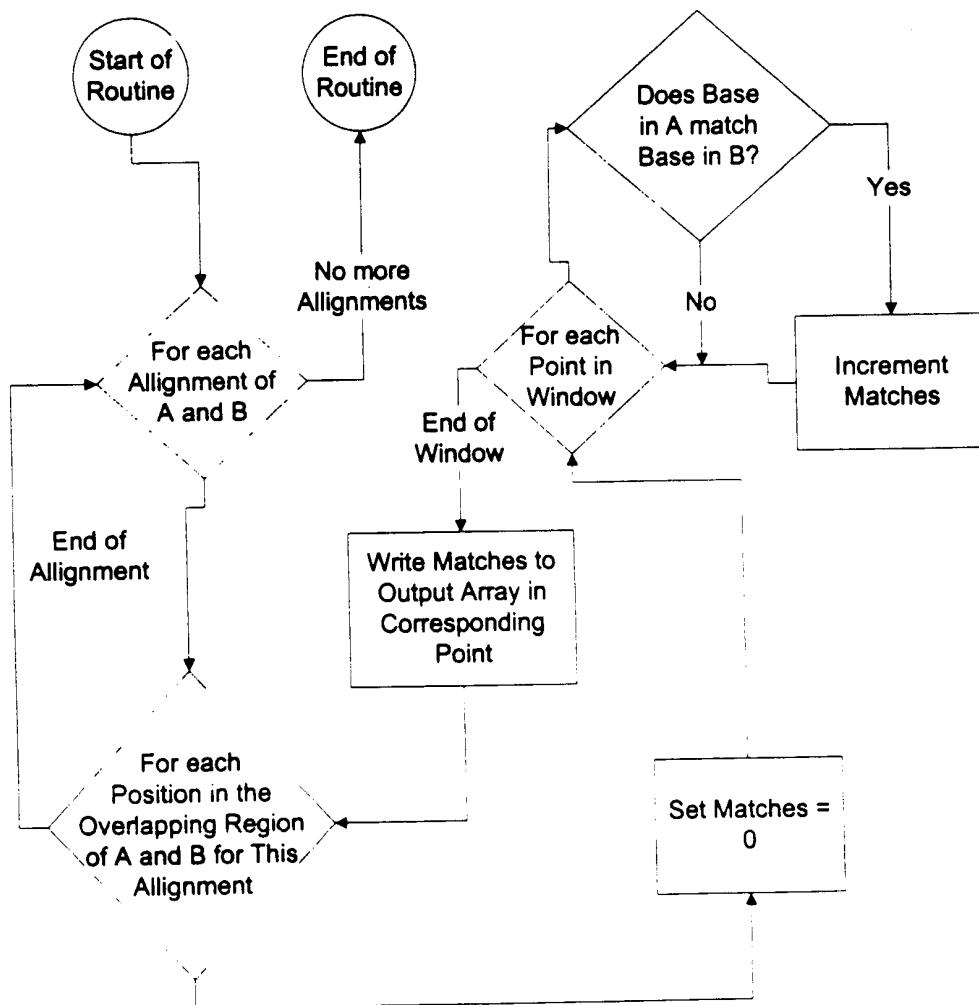
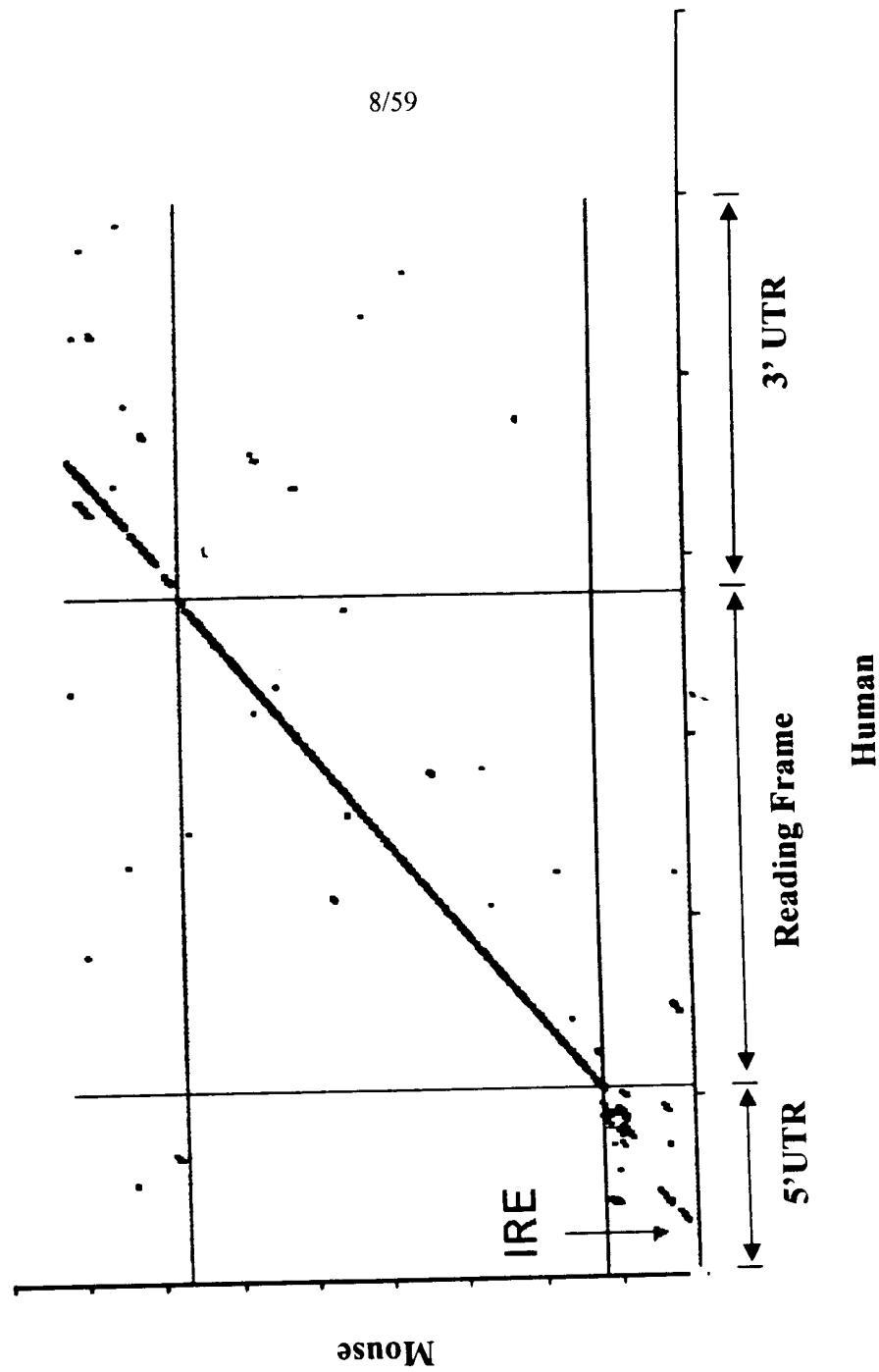


FIGURE 5C

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Figure 6



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Figure 7

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Self Complementarity Comparisons

13 ortholog overlay

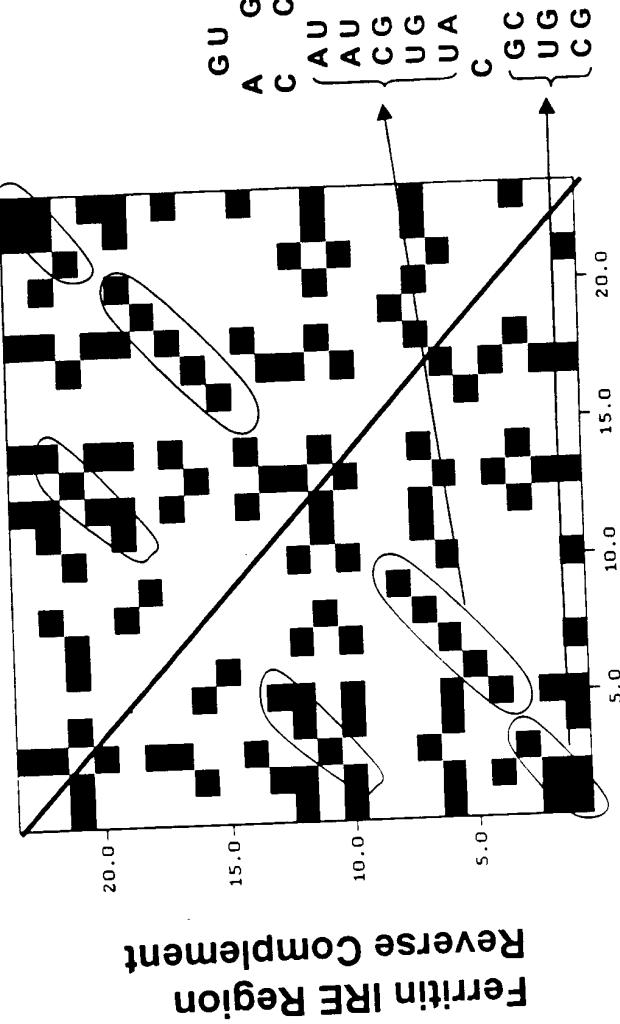
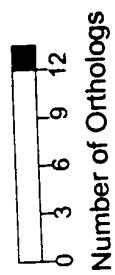
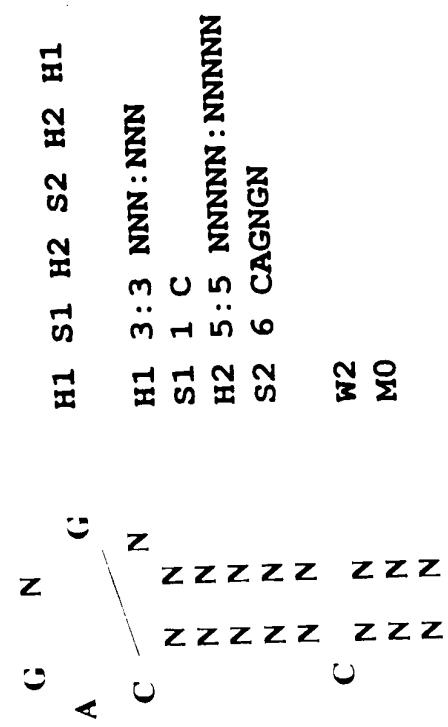


Figure 8



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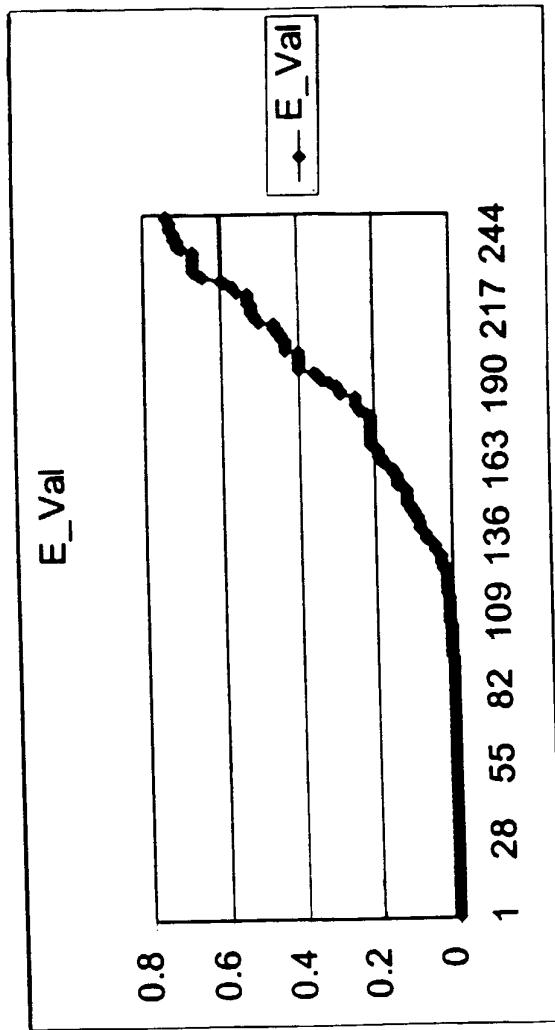
Figure 9



**IRE
Stem-loop Model**

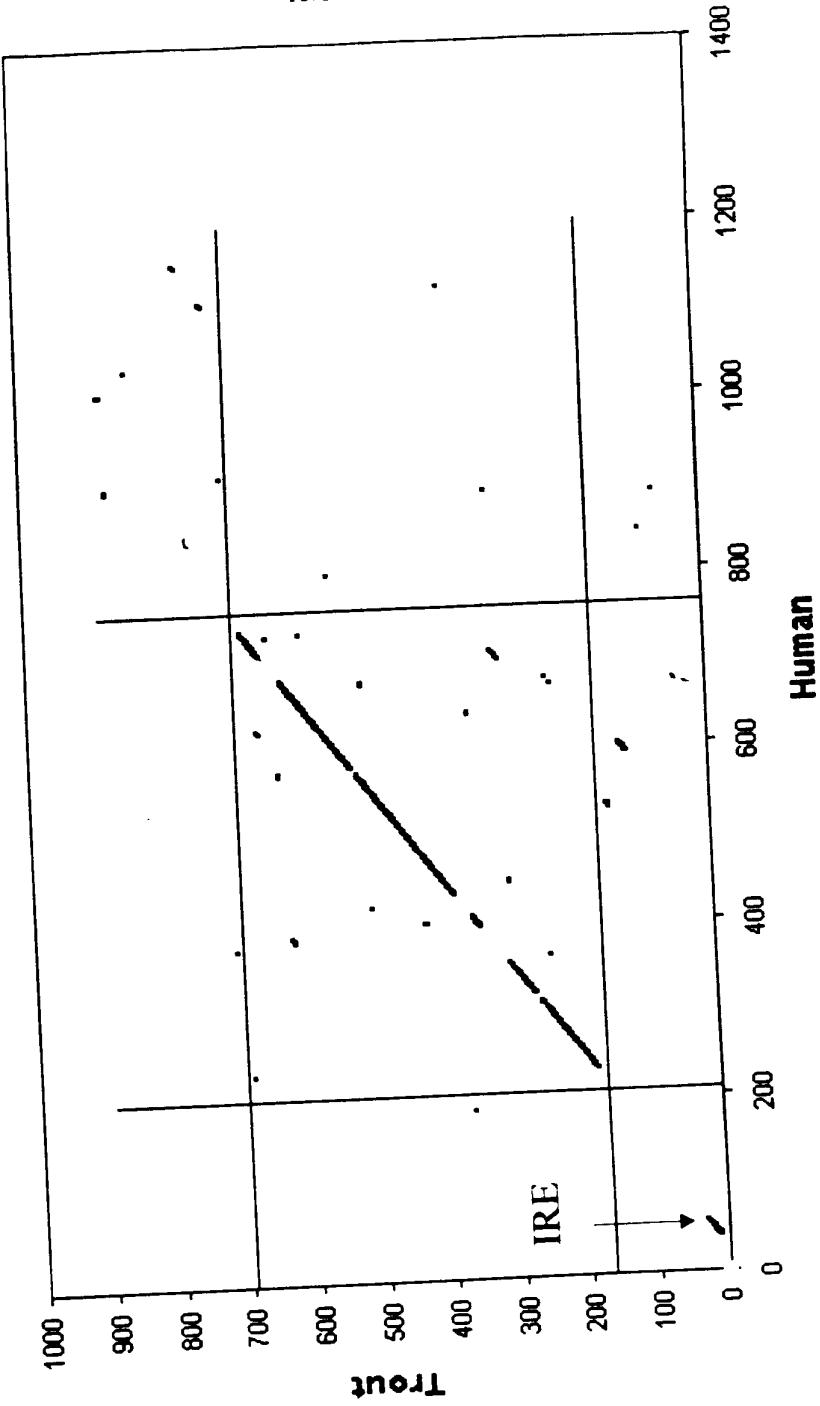
12/59

Figure 10



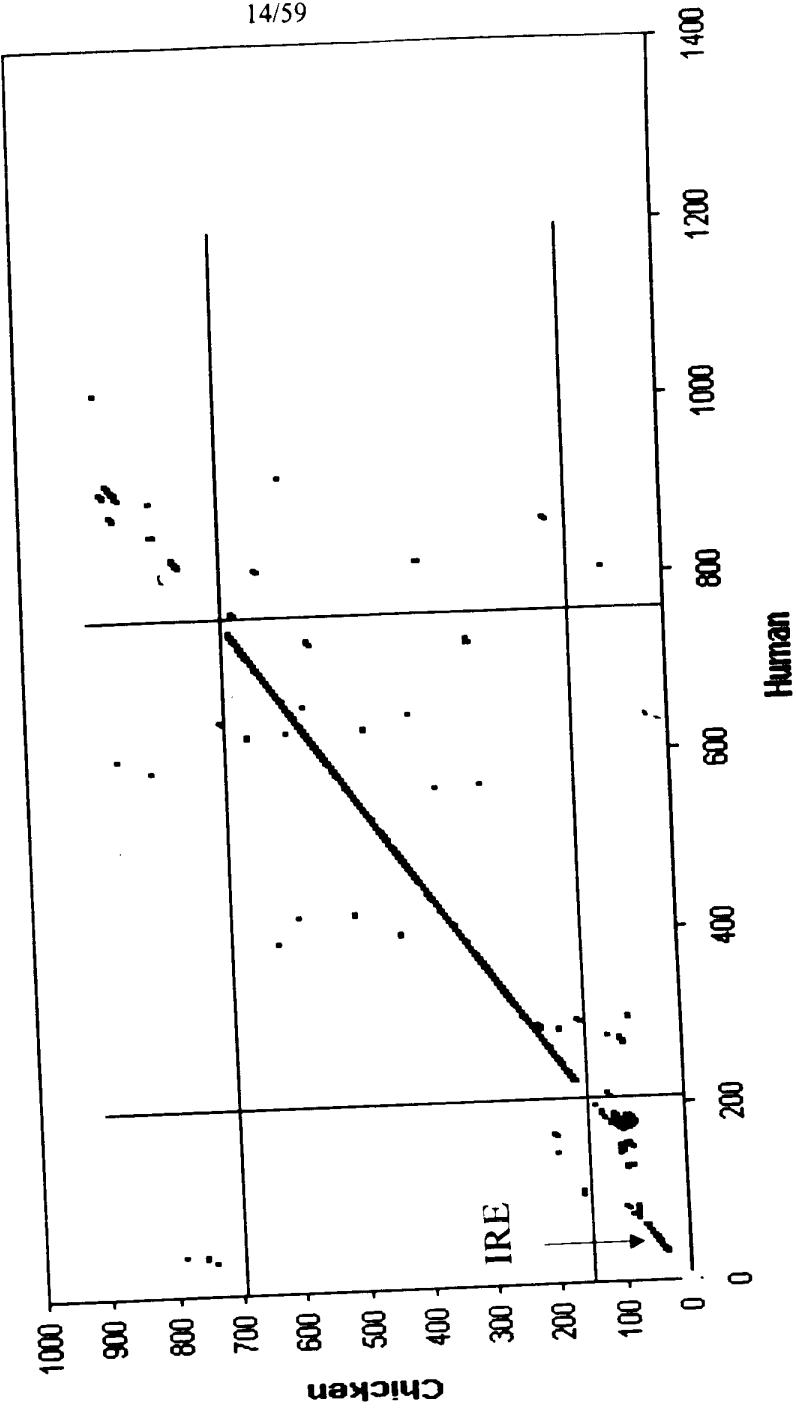
13/59

Figure 11



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Figure 12



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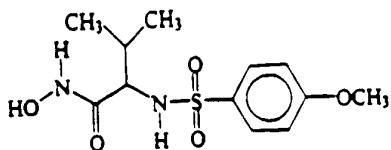
G-U
 A G A G C C C C C C C C C C C C C C C C
 C C C C A-U
 A-U A-U A-U C-G C-G U-G U-A
 C-G U-A U-A U-A C-G G-C U-G C-G U-G U-G U-G U-G U-G U-G U-G U-G U-G
 U-G C-G HAMSTER CHICKEN TROUT SALMON
 C-G HUMAN PIG RAT
 HAMSTER
 MOUSE
 RAT
 CHICKEN
 TROUT
 SALMON
 XENOPUS
 FROG
 FLY
 MOSQUITO

| | NO | NO | Yes | Yes | Yes | NO | NO |
|----------|----|----|-----|-----|-----|----|----|
| HUMAN | NO | NO | Yes | Yes | Yes | NO | NO |
| PIG | NO | NO | Yes | Yes | Yes | NO | NO |
| HAMSTER | | | | | | | |
| MOUSE | | | | | | | |
| RAT | | | | | | | |
| CHICKEN | | | | | | | |
| TROUT | | | | | | | |
| SALMON | | | | | | | |
| XENOPUS | | | | | | | |
| FROG | | | | | | | |
| FLY | | | | | | | |
| MOSQUITO | | | | | | | |

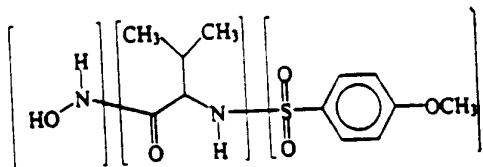
Figure 13

16/59

Compound CI



C₁₂H₁₈N₂O₅S



| | | | |
|-------------------|-------------------|----------------------------------|---|
| | F _i | F _{ii} | F _{iii} |
| Molecular formula | H ₂ NO | C ₅ H ₉ NO | C ₇ H ₁₀ O ₃ S |

Figure 14

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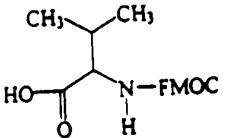
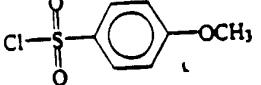
Addition of fragments to yield compounds

Table

| Fragment Identifier | Structure | Name | Molecular formula | Other |
|---------------------|-----------|---------------|--|-------|
| F _i | | Hydroxylamine | H ₂ NO | ... |
| F _{ii} | | Amino acid | C ₅ H ₉ NO | ... |
| F _{iii} | | Sulfonyl | C ₇ H ₇ O ₃ S | ... |

Figure 15

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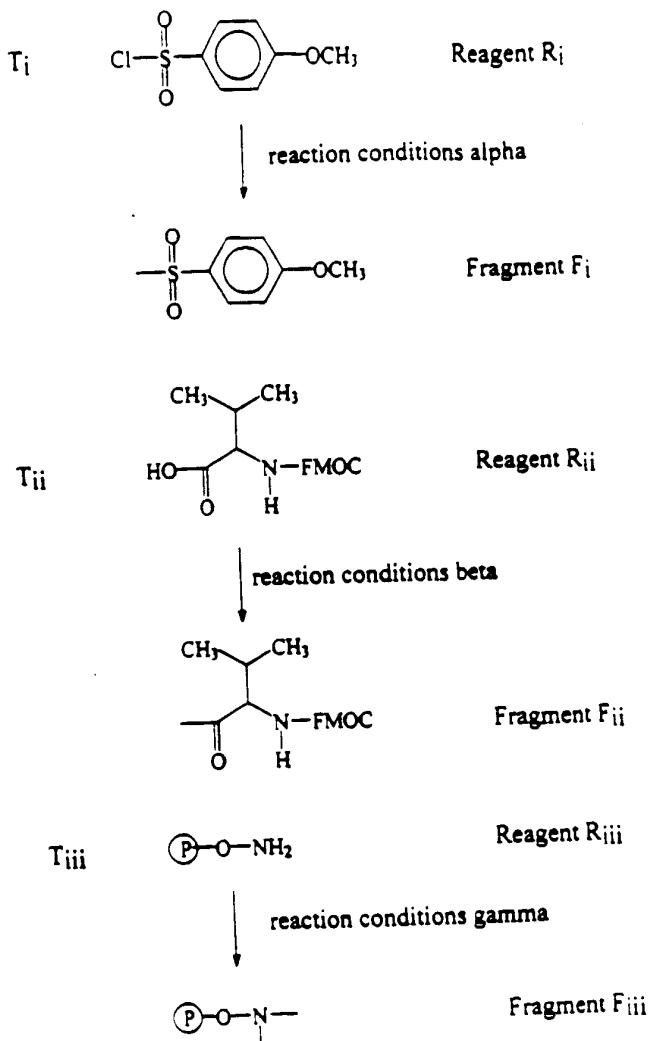
| Reagents | Identifier | Name | Properties |
|---|------------------|----------------------------|------------|
| $\text{H}-\text{O}-\text{NH}_2$ or $\textcircled{P}-\text{O}-\text{NH}_2$ | R _i | Hydroxylamine | ... |
|  | R _{ii} | FMOC blocked amino acid | ... |
|  | R _{iii} | Sulfonylchloride | ... |

\textcircled{P} = Solid support

Figure 16

19/59

Transformation



\textcircled{P} = Solid support

Figure 17

20/59

Common Fragment / Different Reagents and Transformations

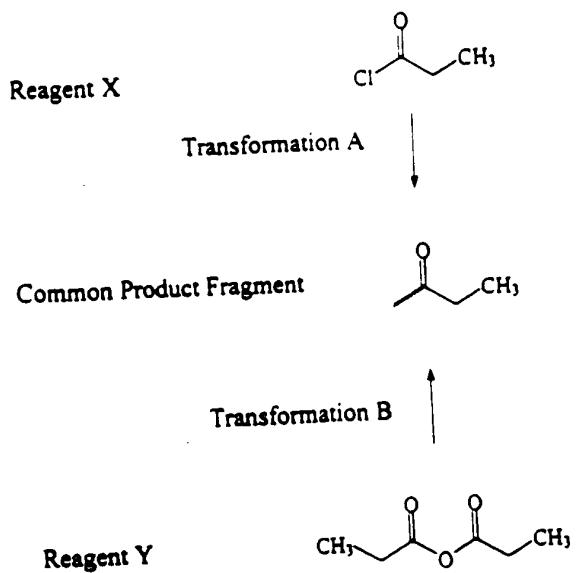


Figure 18

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Common Fragment / Different Reagents and Transformations

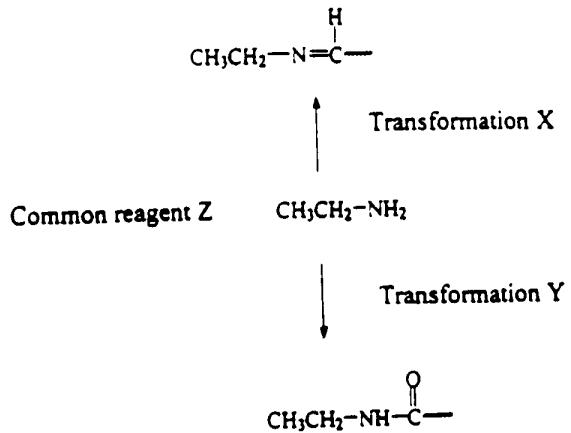


Figure 19A

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Common Reagent

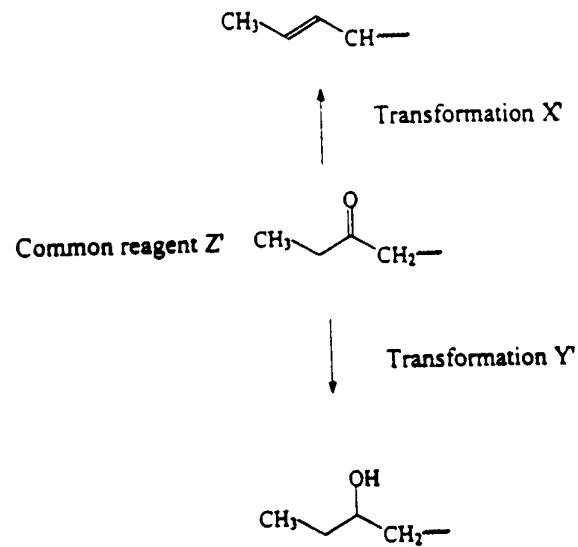


Figure 19B

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Symbolic addition of fragments to yield compound

Symbolic Structure Symbolic Identifier Molecular formula

Fragment



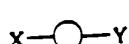
F_i'

C₀H₀N₀W ...



F_{ii}'

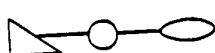
C₀H₀N₀W ...



F_{iii}'

C₀H₀N₀W ...

Compound



C₁'

C₀H₀N₀W ...

Molecular formula F_i'

+

Molecular formula F_{ii}'

+

Molecular formula F_{iii}'

= Molecular formula C₁'

Figure 20

24/59

Symbolic Reagent Table

| <u>Identifier</u> | <u>Name</u> | <u>Structure</u> | <u>Molecular formula</u> |
|-------------------|-------------|------------------|--------------------------|
| R1 | xxx | | xxx |
| R2 | ... | | ... |
| R3 | ... | | ... |
| R4 | ... | | ... |
| R5 | ... | | ... |
| R6 | ... | | ... |
| R7 | ... | | ... |
| R8 | ... | | ... |
| R9 | ... | | ... |
| R10 | ... | | ... |

Figure 21

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Symbolic Fragment Table

| <u>Identifier</u> | <u>Symbolic Structure</u> | <u>Molecular formula</u> | <u>Molecular Weight</u> |
|-------------------|---------------------------|--------------------------|-------------------------|
| F1 | | xxx | xxx |
| F2 | | ... | ... |
| F3 | | ... | ... |
| F4 | | ... | ... |
| F5 | | ... | ... |
| F6 | | ... | ... |
| F7 | | ... | ... |
| F8 | | ... | ... |

Figure 22

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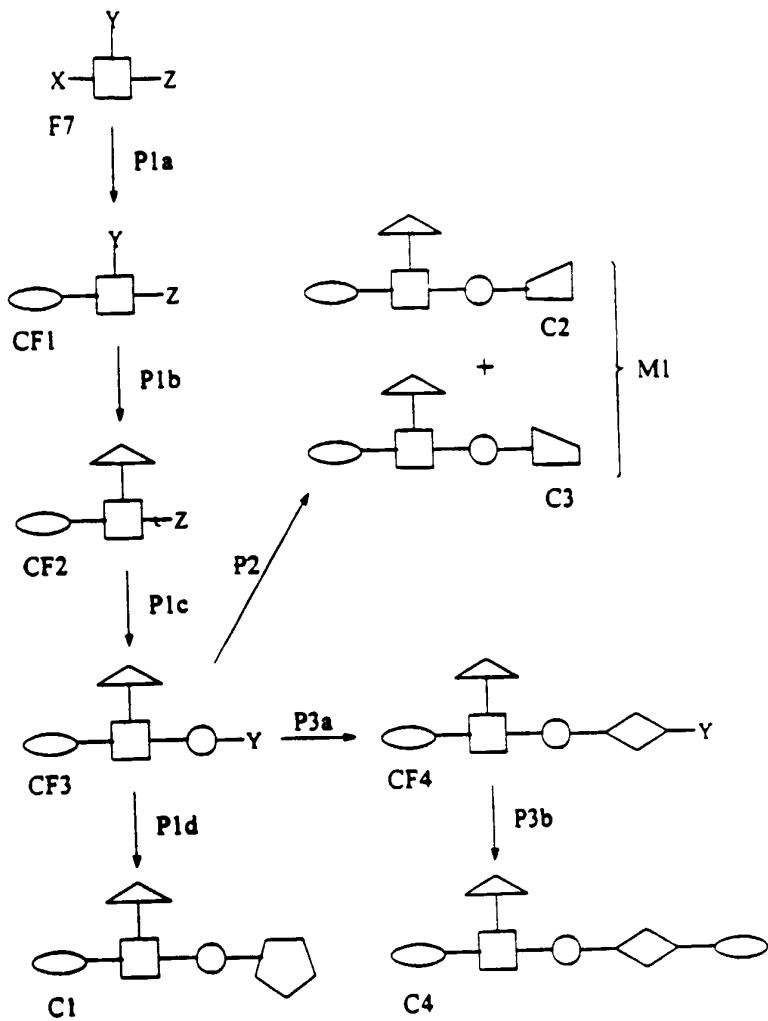
Symbolic Transformation Table

| <u>Identifier</u> | | <u>Symbolic Reactions</u> | <u>Reagent</u> |
|-------------------|----|--|-----------------------|
| T1 | F1 |  $\xleftarrow{R1}$ | conditions α |
| T2 | F2 |  $\xleftarrow{R2}$ | conditions β |
| T3 | F3 |  $\xleftarrow{R3}$ | conditions α |
| T4 | F3 |  $\xleftarrow{R4}$ | conditions α |
| T5 | F4 |  $\xleftarrow{R5}$ | conditions α |
| T6 | F5 | $X-\text{O}-Y \xleftarrow{R6}$ | conditions ϵ |
| T7 | F5 | $X-\text{O}-Y \xleftarrow{R7}$ | conditions α |
| T8 | F6 |  $\xleftarrow{R8}$ | conditions α |
| T9 | F7 |  $\xleftarrow{R9}$ | conditions γ |
| T10 | F8 |  $\xleftarrow{R10}$ | conditions γ |

Figure 23

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Single Compounds and Mixtures



P = synthetic path CF = complex fragment
F = fragment M = mixture
C = compound

Figure 24

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Mixture 2

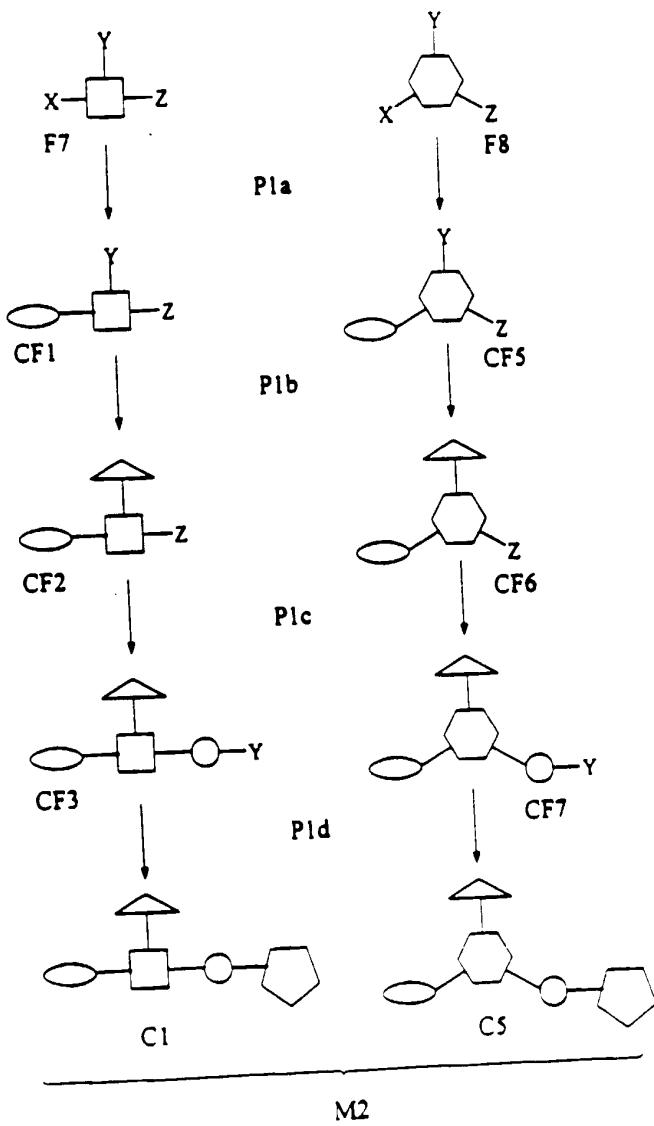


Figure 25

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Mixture 3

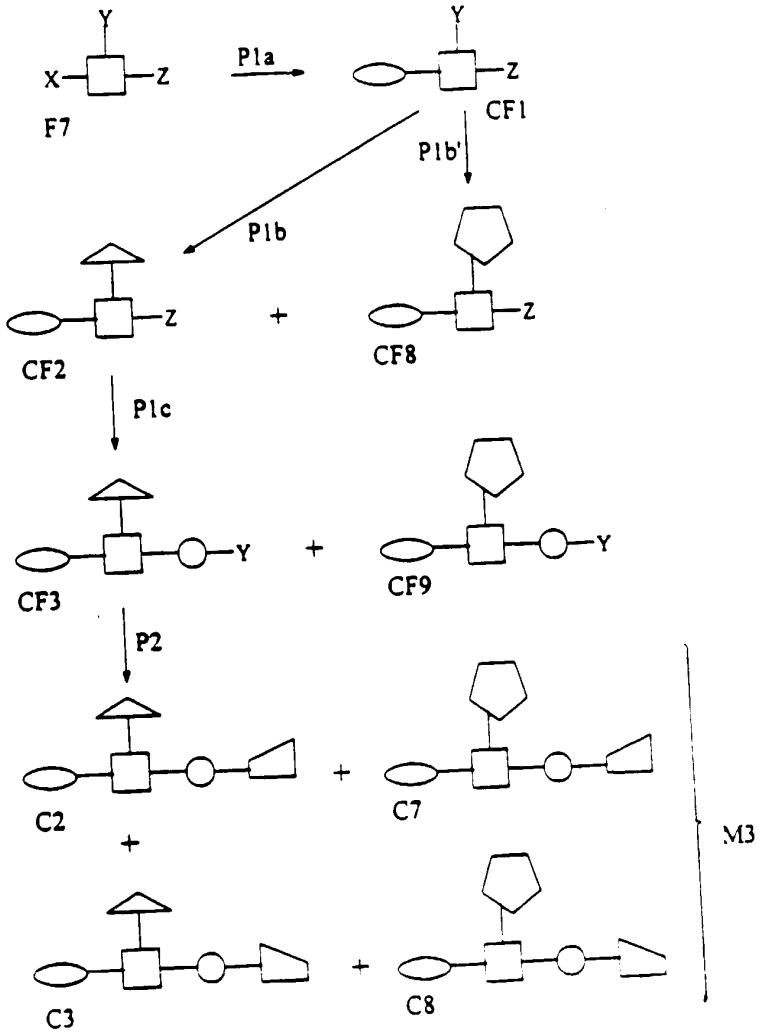


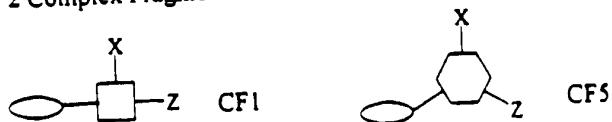
Figure 26

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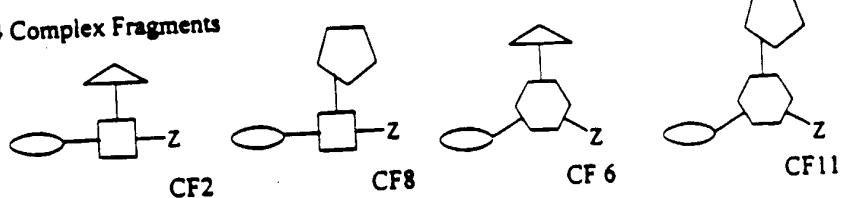
Mixture 4
2 Starting Fragments



2 Complex Fragments



4 Complex Fragments



8 Complex Fragments

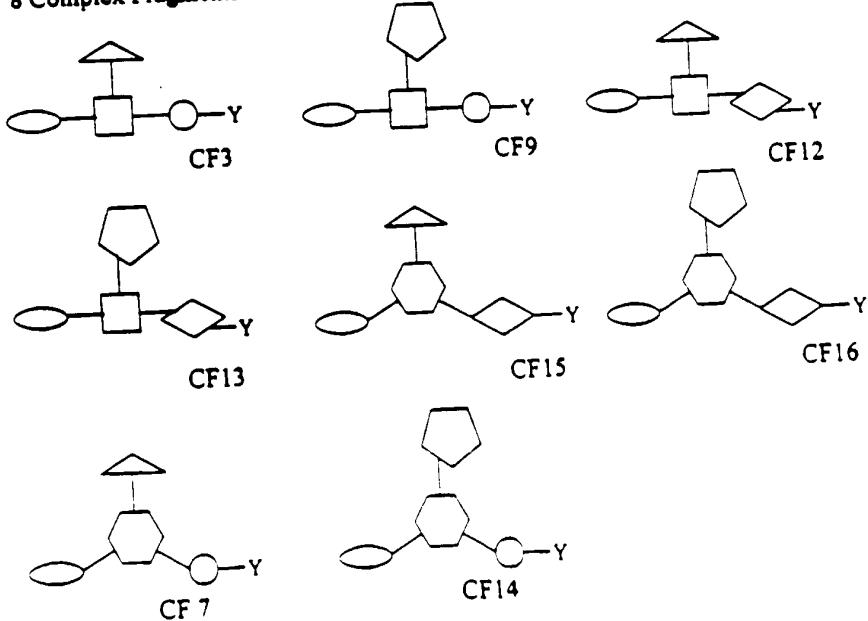


Figure 27A

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Mixture 4 (continued)

16 compounds

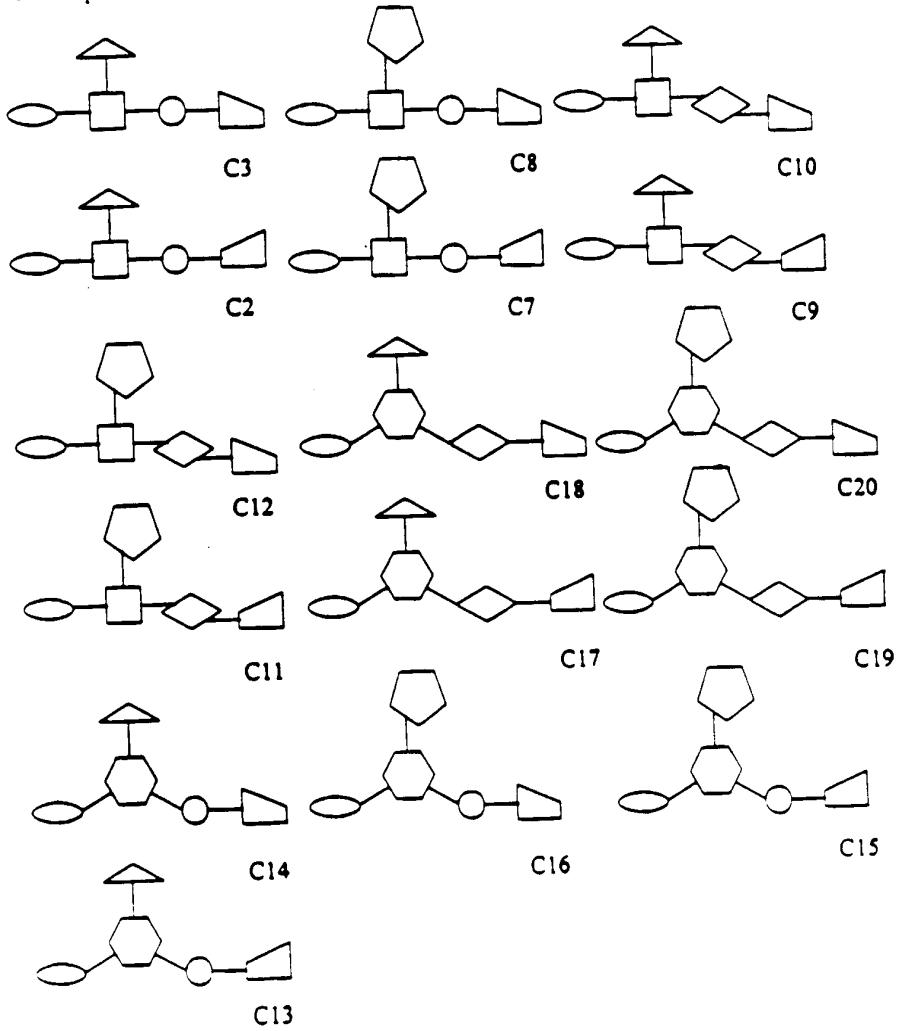


Figure 27B

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Tracking Table for Compound C1

(a) By Fragments:

| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
|----------|------------|------------|
| F7 | | |
| | F2 | |
| | F1 | |
| | F5 | |
| | | F3 |

(b) By Transformations:

Synthesis Path 1

| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
|----------|------------|------------|
| T9 | | |
| | T2 | |
| | T1 | |
| | T6 | |
| | | T3 |

Synthesis Path 2

| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
|----------|------------|------------|
| T9 | | |
| | T2 | |
| | T1 | |
| | T7 | |
| | | T3 |

Synthesis Path 3

| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
|----------|------------|------------|
| T9 | | |
| | T2 | |
| | T1 | |
| | T6 | |
| | | T4 |

Synthesis Path 4

| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
|----------|------------|------------|
| T9 | | |
| | T2 | |
| | T1 | |
| | T7 | |
| | | T4 |

Figure 28

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Tracking Table

Tracking M1

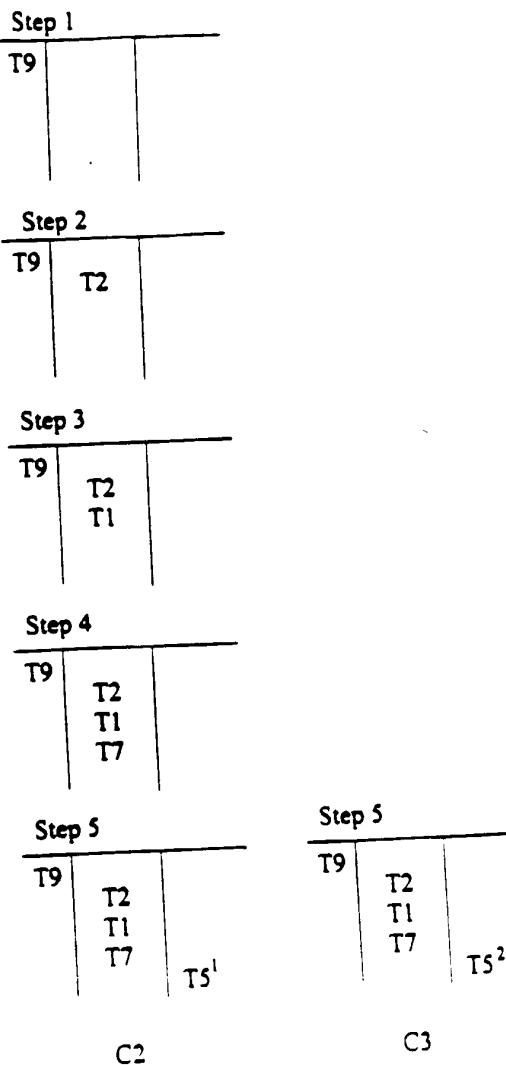


Figure 29

Docket # IBIS-0007 Serial No.: 09/076 404
 Title: REGULATION OF MOLECULAR INTERACTION SITES ON RNA
 AND OTHER MOLECULES
 Inventor: Peter G. and Griffey, Stanley T. Crooke,
 Re: U.S. Patent Office, Attorney: Kramer Mohan and Steve Hofstader
 Attorney: Paul R. Legarda Attorney Phone No.: 215-564-8906
 Sheet 34 of 59

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Tracking Table

Tracking M2

| Step 1 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T9 | | |

| Step 1 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T10 | | |

| Step 2 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T9 | T2 | |

| Step 2 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T10 | T2 | |

| Step 3 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T9 | T2 T1 | |

| Step 3 | | |
|----------|------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T10 | T2 T1 | |

| Step 4 | | |
|----------|----------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T9 | T2 T1 T7 | |

| Step 4 | | |
|----------|----------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T10 | T2 T1 T7 | |

| Step 5 | | |
|----------|----------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T9 | T2 T1 T7 | T4 |

| Step 5 | | |
|----------|----------------|------------|
| <u>n</u> | <u>n+1</u> | <u>n+2</u> |
| T10 | T2 T1 T7 | T4 |

C1

C5

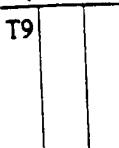
Figure 30

35/59

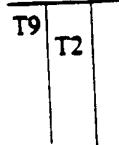
Tracking Table

Tracking M3

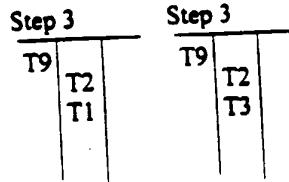
Step 1



Step 2

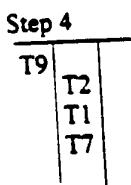


Step 3

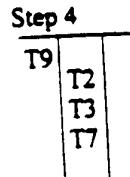


Step 3

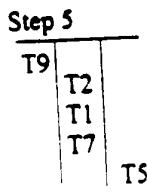
Step 4



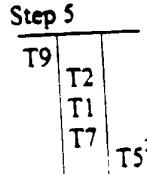
Step 4



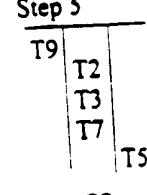
Step 5



Step 5



Step 5



Step 5

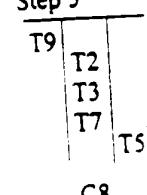


Figure 31

Docket No. IBIS-0007 Serial No. 09/076,404
Title: REGULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER NUCLEIC ACID MOLECULES
Inventors: Michael J. Pelsue, Michael J. Grifley, Stanley T. Crooke,
Rajendra Sarpal, Michael J. Grifley, Venkatesan Mohan and Steve Hofstadler
Attorneys: Paul J. Legault
Attorney Phone No.: 215-564-8906
Sheet 36 of 59

36/59

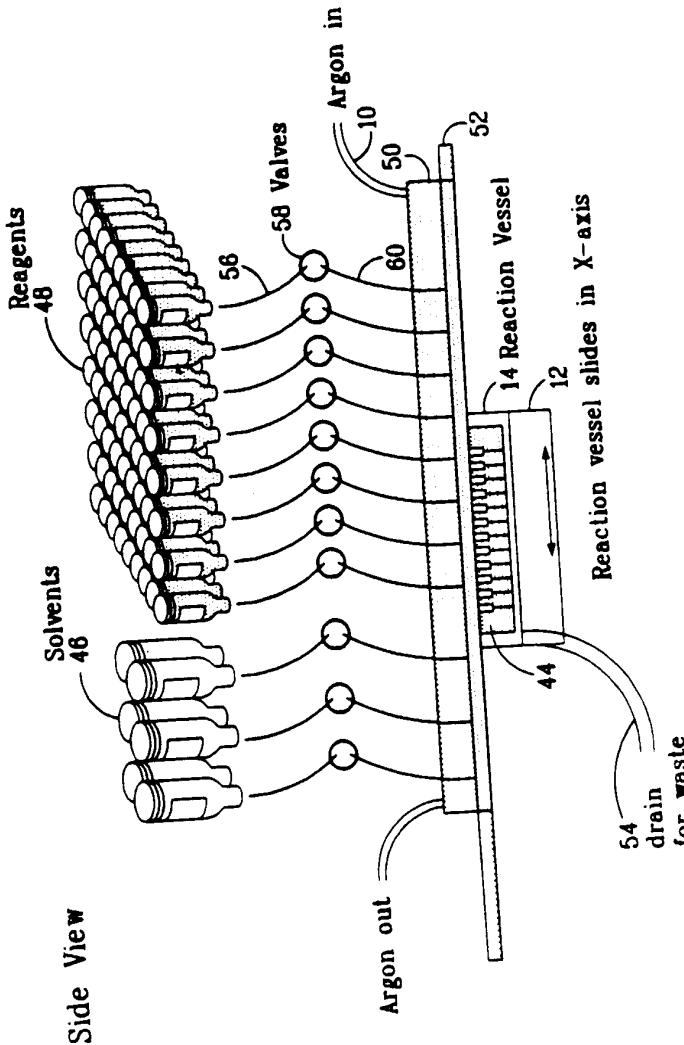


Figure 32

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Top View

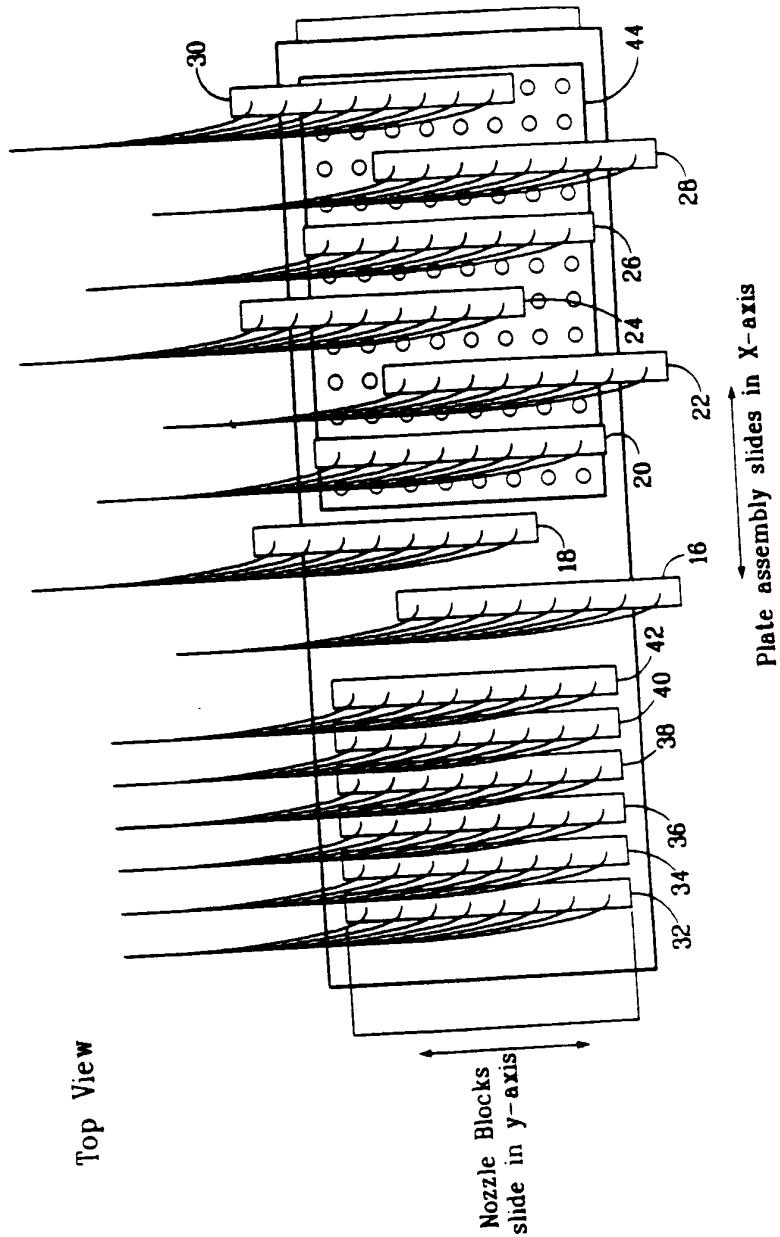


Figure 33

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Synthesis of hydroxamic acids from hydroxylamine resin

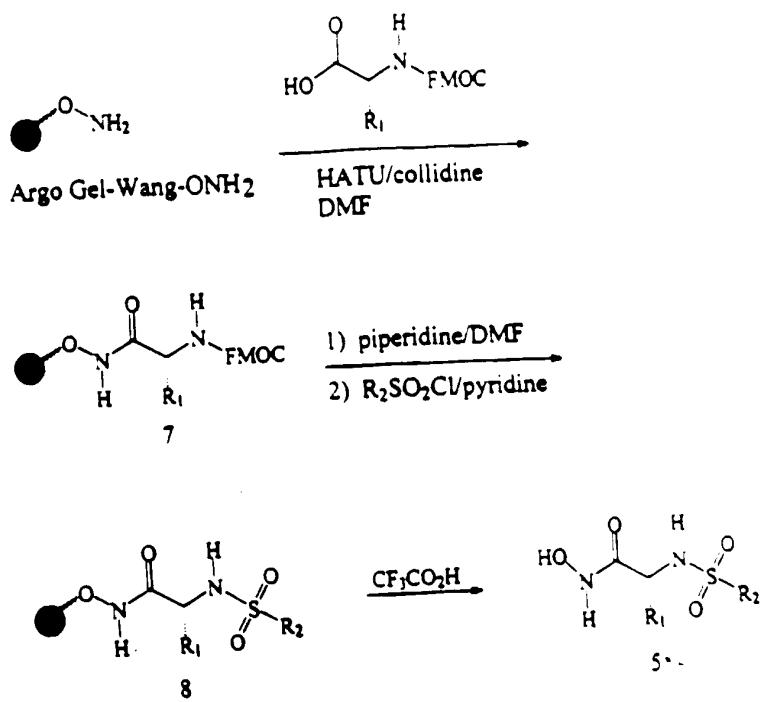


Figure 35

DocID: IBIS-0007 Serial No.: 09/076,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventor: Daniel E. Egan, Richard Griffey, Stanley T. Crooke,
Randy L. Johnson, Michael S. Katze, Raman Mohan and Steve Hofstadler
Assignee: Genentech, Inc. Attorney Phone No.: 215-564-8906
Priority: Feb 19, 1990
Sheet 46 of 59

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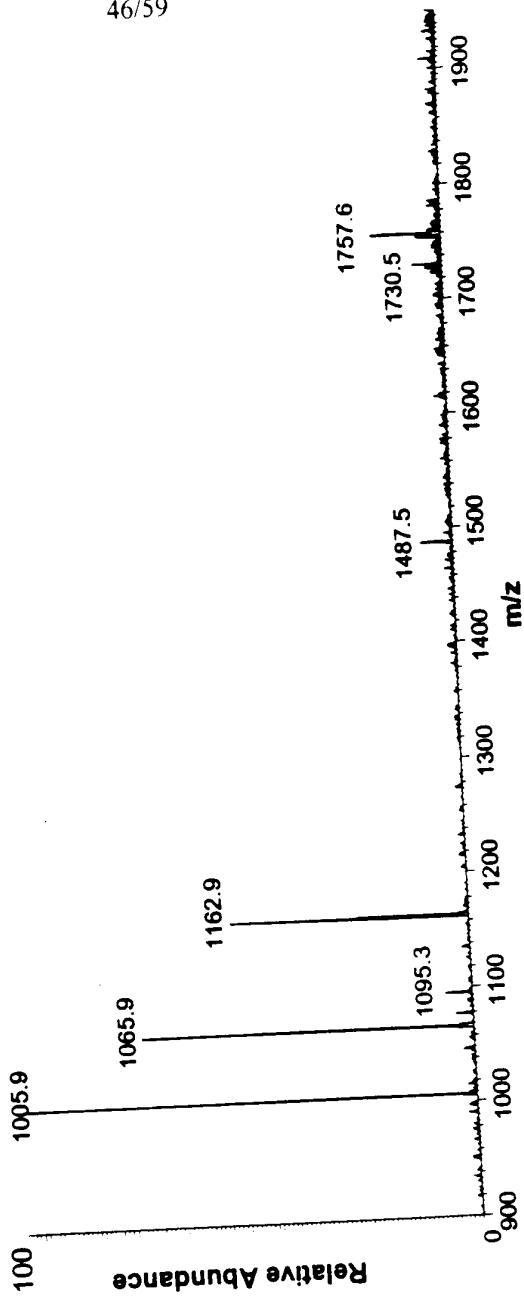


Figure 41A

DocID: IBIS-0007 Serial No.: 09/076,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventor: David C. Crooke, K. Griffey, Stanley T. Crooke,
R. K. Lautenbacher, K. M. Katraman Mohan and Steve Hofstadler
Attorney: Paul K. Englund Attorney Phone No.: 215-564-8906
Sheet 47 of 59

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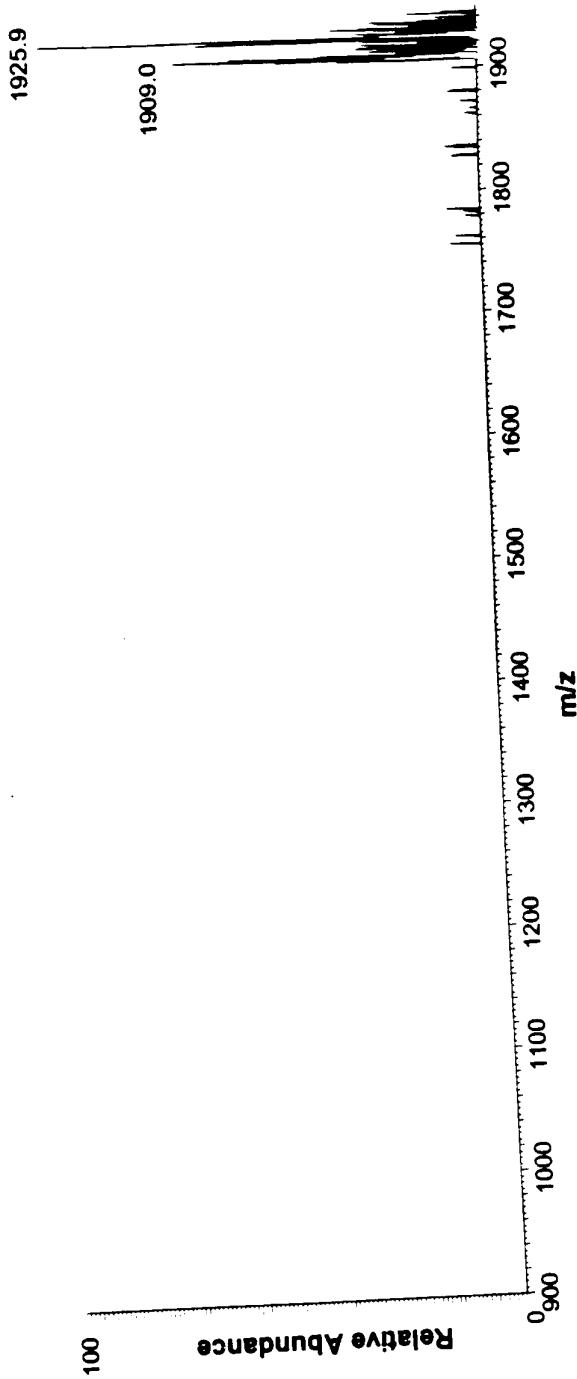


Figure 41B

Document IBIS-0007 Serial No.: 09/076,404
Title: CALCULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER MOLECULES
Inventor: David E. Griffey, Stanley T. Crooke,
Ranjan C. Achraman and Steve Hofstadler
Attorney: Pacific Legal, Inc.
Attorney Phone No. 215-564-8906
Sheet 48 of 59

48/59

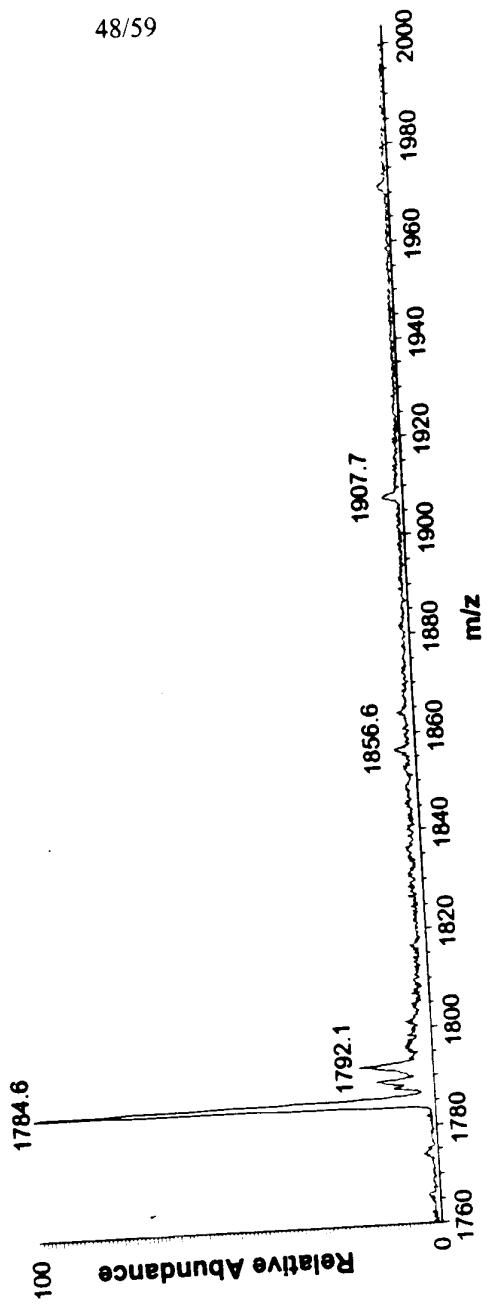


Figure 42.A

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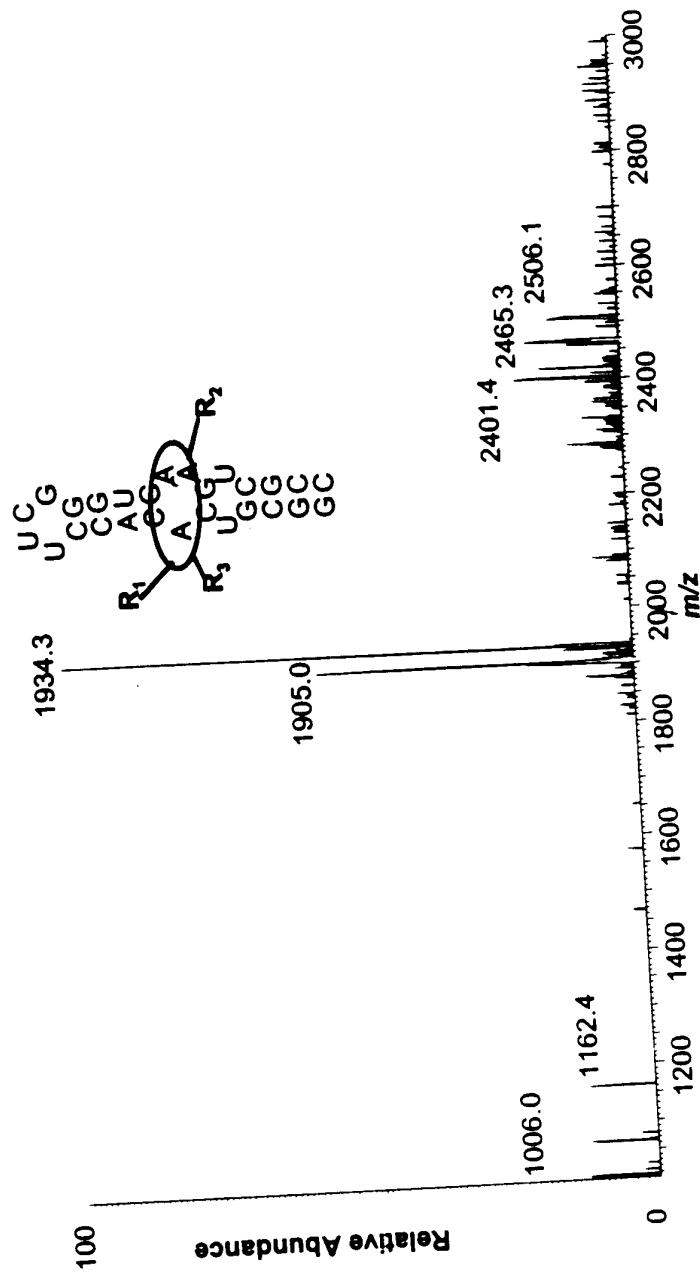


Figure 46

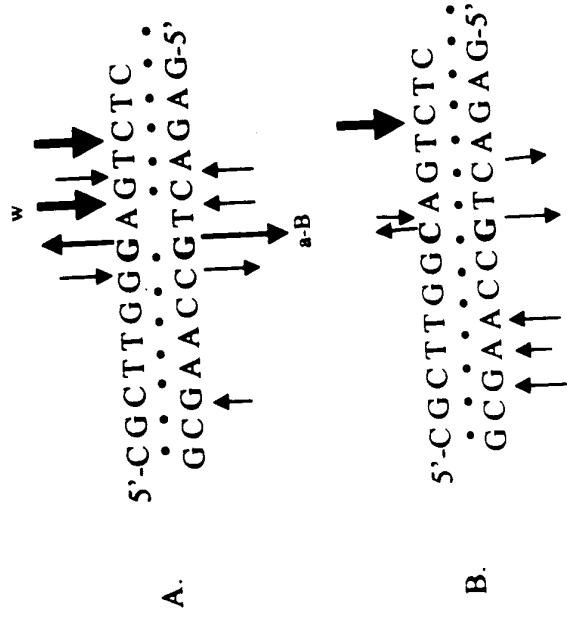


Figure 47

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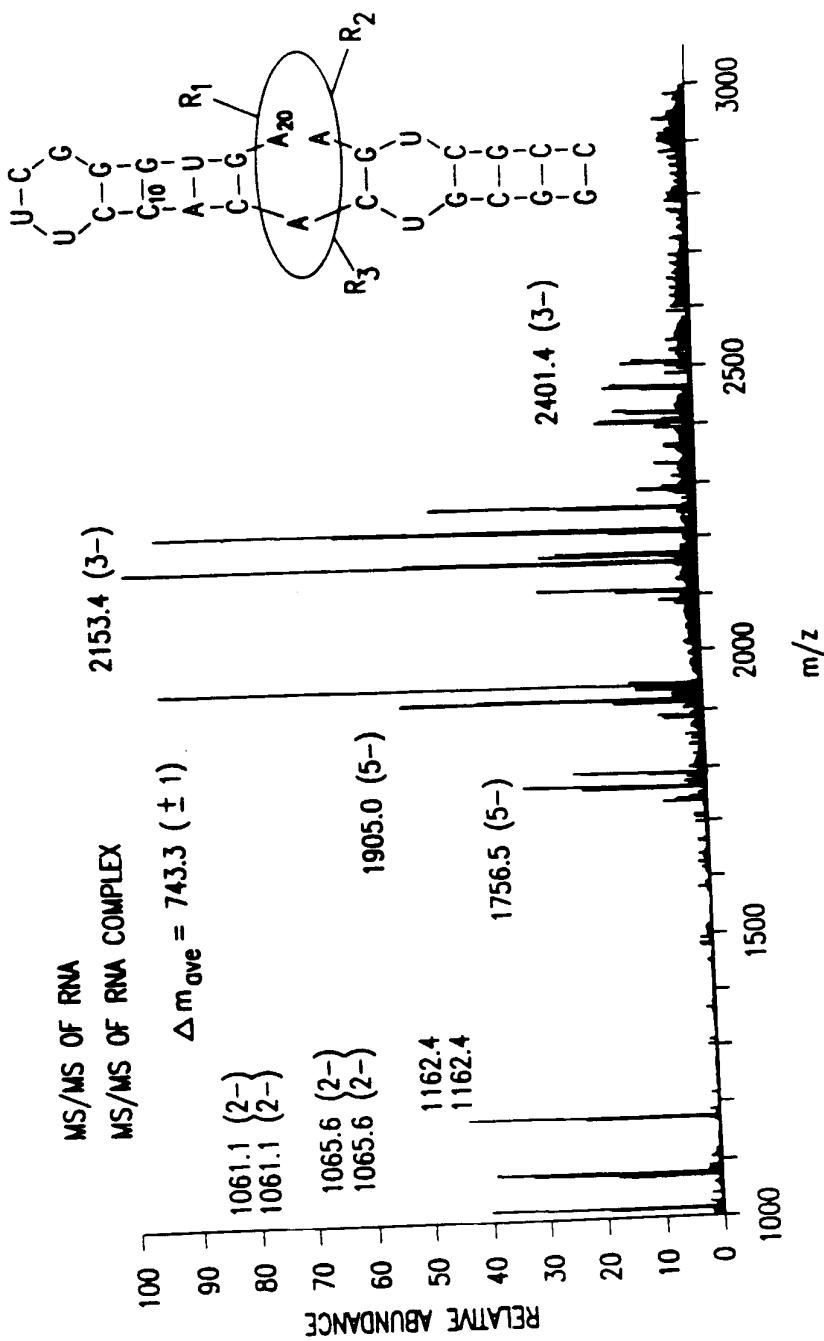


Figure 50

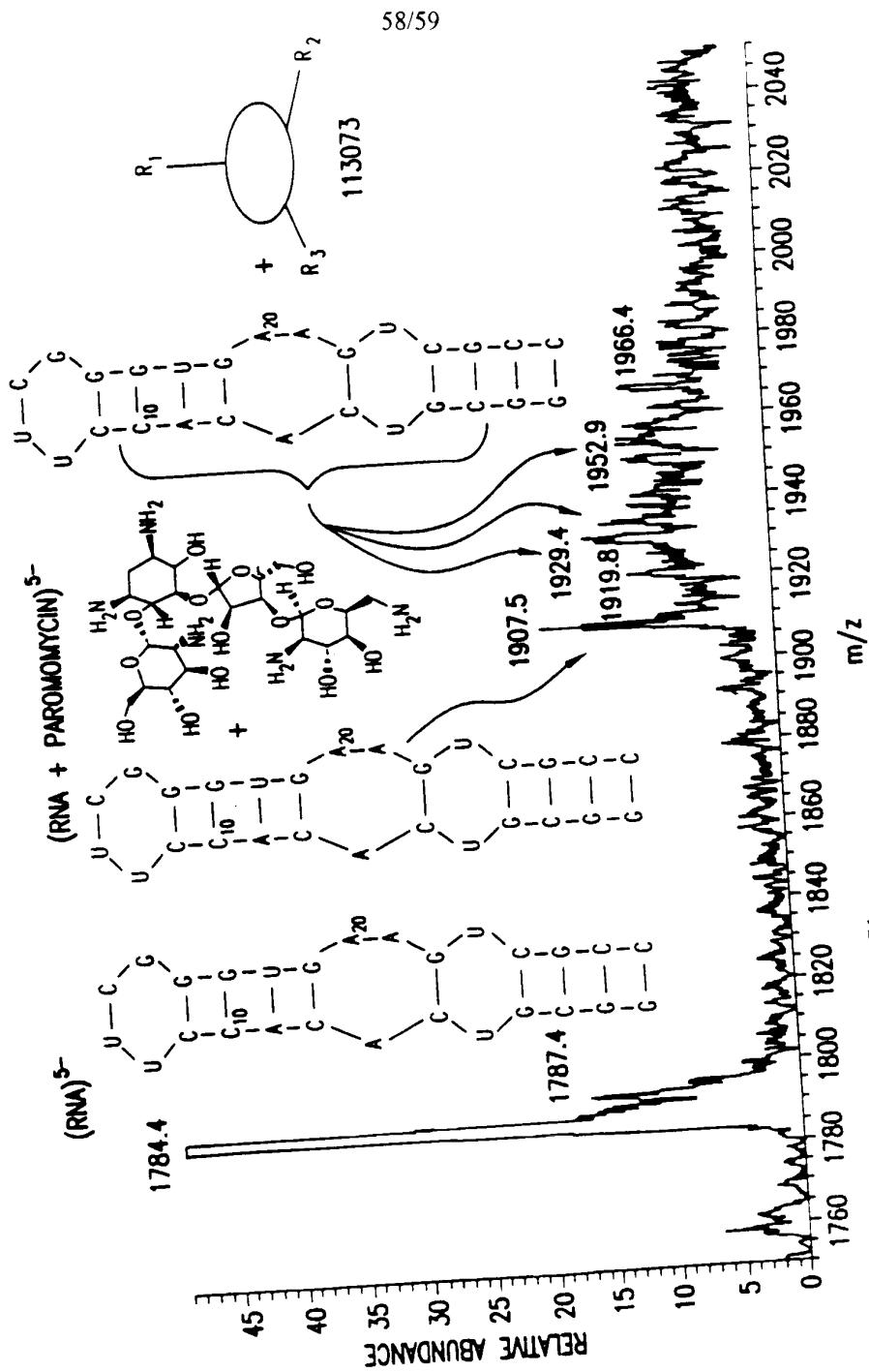


Figure 51

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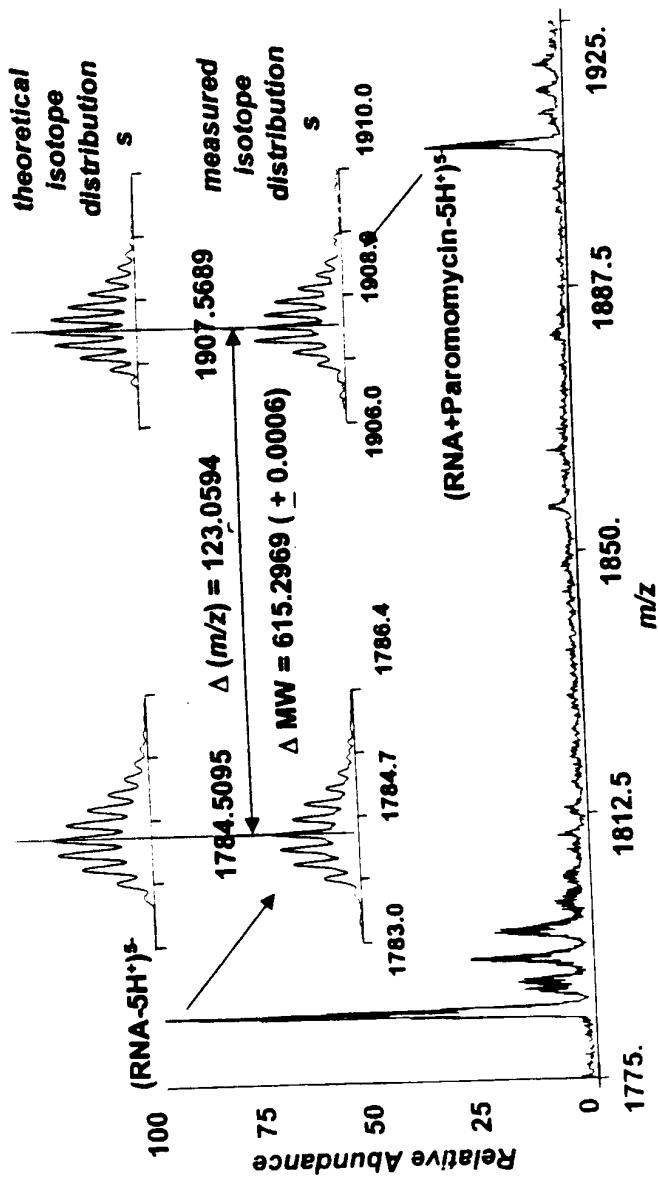


Figure 52